

## REMARKS/ARGUMENTS

Claims 1, 5, 6, 10, 16-18 and 20-32 are currently pending and under consideration.

### **1. The Rejection under 35 U.S.C. § 102(b) in view of Nakamichi is in error.**

Claims 10, 16-18 and 23-32 are rejected under 35 U.S.C. § 102(b) as, allegedly, anticipated by European Patent Application Publication No. 0 580 860 A1 to Nakamichi *et al.* (“Nakamichi”). According to the Examiner, Nakamichi teaches a method of manufacturing a pharmaceutical solid dispersion, produced without heating chemicals and polymeric carriers above their respective melting points.

Applicants respectfully disagree. The rejected claims are directed to co-extruded controlled release matrices produced by a specified method, and to co-extruded controlled release matrices comprising at least one starch in which the starch is vitrified. However, the solid dispersions of Nakamichi are not controlled released dispersions. Applicants invite the Examiner’s attention to Figures 1, 3, 5, 6, 8, 10 and 12 which show that the solid dispersions of Nakamichi either release essentially no active ingredient or release essentially all of the active ingredient quickly.

In order for a reference to anticipate a claim, each and every element of the claim must be disclosed in that one reference. *Orthokinetics, Inc. v. Safety Travel Chairs, Inc.*, 806 F.2d 1565 (Fed. Cir. 1985). “Anticipation under Section 102 can be found only if a reference shows exactly what is claimed. . .” *Structural Rubber Prod. Co. v. Park Rubber Co.*, 749 F.2d 707 (Fed. Cir. 1984). None of the pending claims is explicitly anticipated by the disclosure of Nakamichi since none of the solid dispersions taught by Nakamichi are controlled release dispersions.

In view of the foregoing, Applicants respectfully request withdrawal of this rejection under 35 U.S.C. § 102(b) in view of Nakamichi.

### **2. The Rejection under 35 U.S.C. § 102(b) in view of Lentz is in error.**

Claims 10, 16, 17, and 23-32 are rejected under 35 U.S.C. § 102(b), allegedly, as anticipated by International Patent Publication No. WO 92/15285 to Lentz *et al.* (“Lentz”). Applicants respectfully disagree.

In order for a reference to anticipate a claim, each and every element of the claim must be disclosed in that one reference. *Orthokinetics, Inc. v. Safety Travel Chairs, Inc.*, 806 F.2d 1565 (Fed. Cir. 1985). “Anticipation under Section 102 can be found only if a reference shows

exactly what is claimed. . .” *Structural Rubber Prod. Co. v. Park Rubber Co.*, 749 F.2d 707 (Fed. Cir. 1984). None of the rejected claims, directed to controlled release matrices, is explicitly anticipated by the disclosure of Lentz since Lentz does not disclose such controlled release matrices. Applicants maintain their position that the Examiner is improperly combining one teaching of Lentz with regard to processing starch and combining the processed starch with an active agent and the teaching in Lentz with regard to co-extruding previously processed starch with an active agent. The present claims are limited to compositions produced by co-extrusion which are different from the sole co-extruded composition of Lentz. The Examiner asserts that this example is not meant to be limiting, but Applicants assert that it fully exemplifies the disclosure of Lentz with regard to co-extruding a pharmaceutically active agent with the molecularly dispersed starch (MDS) taught in Lentz. Even though both Lentz and the present invention teach destructure of starch by way of extrusion, the nature of the destructured starch obtained is different since the molecularly dispersed starch of Lentz is soft and rubbery and, thus, above glass transition temperature. In fact, Lentz teaches at page 14, lines 6-25, that it is preferred that the process heats the starch above the glass transition temperature.

In contrast, the extruded matrices obtained by the present invention are vitrified, *i.e.*, rigid and, thus, their temperature never exceeded the glass transition temperature and preferably remains below the glass transition temperature, as specified in the claims.

In view of the foregoing, Applicants submit that the claimed co-extruded compositions are not anticipated by Lentz, and, therefore, respectfully maintain their request that this Section 102(b) rejection be withdrawn.

### **3. The Rejection under 35 U.S.C. § 103(a) in view of Nakamichi is in error.**

Claims 1, 5, 6, 10, 16-18, 20-32 are rejected under 35 U.S.C. § 103(a), allegedly, as obvious over European Patent Application Publication No. 0 580 860 A1 to Nakamichi *et al.* (“Nakamichi”). The Examiner alleges that Nakamichi is silent on certain parameters of the extrusion process but that it would have been obvious for one skilled in the art to optimize such parameters to obtain the desired product.

Applicants respectfully disagree. In order to establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981, 180 U.S.P.Q. 580 (CCPA 1974). Additionally, the Supreme Court, in *KSR International Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 82 U.S.P.Q. 1385 (2007), affirmed that “a patent composed of several elements is not proved obvious merely by demonstrating that

each of its elements was, independently, known in the prior art,” and that it is “important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does...because inventions in most, if not all, instances rely upon building blocks long since uncovered, and claimed discoveries almost of necessity will be combinations of what, in some sense, is already known.” *KSR*, S.Ct. at 1741, 82 U.S.P.Q.2d at 1396. Further, under *KSR*, “a court must ask whether the improvement is more than the predictable use of prior art elements according to their established functions.” *KSR*, S.Ct. at 1740, 82 U.S.P.Q.2d at 1396. The relevant inquiry is whether the prior art suggests the invention and whether the prior art provides one of ordinary skill in the art with a reasonable expectation of success. *In re O’Farrell*, 853 F.2d 894, 7 U.S.P.Q.2d 1673 (Fed. Cir. 1988).

In the instant application, the claims are directed to methods of co-extrusion under specified conditions and to the controlled release matrices that result from the methods of co-extrusion. While Applicants would not dispute that, in certain instances, the optimization of a parameter would be obvious; however, only in cases where the cited prior art teaches not only which parameter to optimize, but also what is the desired product. Applicants submit that the claimed invention is not obvious in view of Nakamichi since Nakamichi does not provide the skilled artisan with the teaching or suggestion of the product to be obtained or the teaching or suggestion of which extrusion parameters to adjust and how to adjust said parameters to achieve the desired product. In the instant case, Nakamichi does not teach or suggest which of the many parameters should be adjusted, if any, *e.g.*, temperature, pressure, amount of water, *etc.*, to achieve the desired result, and Nakamichi does not teach or suggest that a controlled release matrix or a method of obtaining such a controlled release matrix are the desired product. Applicants submit that it would be undue experimentation to try to achieve the claimed invention based on the teachings of Nakamichi. Nakamichi does not provide the person of skill in the art the required reasonable expectation of success to achieve the co-extrusion methods and controlled release compositions claimed in the present application, thus, Nakamichi does not render the claimed invention obvious.

In view of the foregoing, Applicants respectfully maintain their request that the rejection under Section 103(a) in view of Nakamichi be withdrawn.

**4. The Rejection under 35 U.S.C. § 103(a) in view of Lentz is in error.**

Claims 1, 5, 6, 10, 16-18, 20-32 are rejected under 35 U.S.C. § 103(a), allegedly, as anticipated by International Patent Publication No. WO 92/15285 to Lentz *et al.* ("Lentz"). Applicants respectfully disagree.

Applicants, in order not to burden the record, hereby incorporate by reference their remarks made previously with regard to the teachings of Lentz, including the Declaration of Dr. Rein, and address the Examiner's comments made in the current office action.

Applicants note that the Examiner's use of the specific examples in Figure 10 to support his position on overlapping temperatures does not support his position. First, Applicants point out that the claimed methods specifically recite temperatures below 100°C. Thus, three of the four specific examples in Figure 10 of Lentz, 160°C, 130°C, and 100°C, fall outside the claims. Second, the sole temperature below 100°C in Figure 10 is 70°C. However, this temperature does not produce a controlled release matrix, but rather a quick release dispersion. Thus, Lentz teaches extrusion at the sole temperature that falls within the claims produces a quick release dispersion, not a controlled release dispersion. Based on this example, Applicants submit that Lentz also teaches away from the claimed invention.

As submitted previously, the only passage in Lentz that concerns co-extrusion of a pharmaceutically active agent and a starch is on page 17, line 37 to page 18, line 1. However, there are absolutely no details in the Lentz specification to teach one skilled in the art how such a co-extrusion can be carried out, unless the co-extrusion is carried out by the same methodology as Lentz uses to extrude the starch alone. Example 18 in Lentz, however, does provide details for a method of co-extrusion. However, Example 18 teaches co-extrusion of not starch but molecularly dispersed starch (which was previously extruded starch) with an active agent (clotrimazole) and talc. Further, as explicitly stated by Lentz, the resulting co-extruded product is a foamed, rubbery product, which is not a controlled release matrix. The pending claims require that the matrix produced by the method be a vitrified controlled release matrix, *i.e.*, glassy. A foamed, rubbery product is not a glassy vitrified product. Applicants do not find it reasonable to interpret the disclosure of Lentz to include the teaching or suggestion of a controlled-release product produced by co-extrusion below 100°C. Lentz does not teach or suggest a modification of its disclosed method requiring that the temperature at the orifice of the extruder (as well as all other parts of the extruder) during the extrusion process be below 100°C under normal pressure. Lentz does not teach or suggest that the temperature be kept under 100°C, and the only time Lentz actually co-extruded an active agent with its molecularly dispersed starch, no controlled release product was achieved. Indeed, the only disclosed specific

experimental conditions for processing starch are found in Example 1 of Lentz and the molecularly dispersed starch (MDS) produced in Example 1 is used throughout all other experiments, including the co-extrusion experiment in Example 18. Applicants submit that the MDS produced according to Example 1 is, indeed, representative of the MDS used in all other experiments disclosed in Lentz, which MDS is not the same as nor suggestive of the co-extruded compositions of the present invention. Applicants maintain the position that it is unreasonable for the Examiner to extrapolate the disclosure of Lentz to suggest the co-extrusion of starch and an active agent at a die temperature of less than 100°C.

With regard to the Examiner's allegation that the Declaration of Dr. Rein does not fully support the full breadth of the claims, Applicants note that experiments disclosed in the present specification as originally filed provide a temperature profile of 65°C-80°C-98°C, thus encompassing a die temperature of under 100°C. Furthermore, Applicants note that Dr. Rein not only performed an experiment with a temperature profile 80°C-80°C-80°C, but also performed experiments with die temperatures of 97°C, 100°C, 102°C, and 114°C. Thus, the specification as originally filed already provides examples covering co-extrusion at a die temperature of less than 100°C and Dr. Rein subsequently showed by the submitted experimental data that, if one were to co-extrude at a die temperature of less than 100°C, one would obtain vitrified products with controlled release properties. Thus, evidence has been presented that covers the full breadth of the claims.

In view of the foregoing, Applicants respectfully maintain their request that the rejection under Section 103(a) in view of Lentz be withdrawn.

### **CONCLUSION**

Applicants respectfully request that the above-made and remarks of the present Reply be entered and made of record in the file history of the present application. Applicants submit that the presently pending claims fully meet all requirements for patentability and respectfully request that the Examiner's rejections be withdrawn and that the application be allowed.

Applicants request that the undersigned be contacted at (212) 326-3939 if any questions or issues remain.

Respectfully submitted,

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